

- (i) do not occur in the same protein in nature,
  - (ii) do not occur in the same protein in nature in the order in which they are present in the chimeric protein, or
  - (iii) do not occur in nature with the same spacing that is present in the chimeric protein.
41. (Amended) The nucleic acid of claim 40, wherein [the composite binding site is DNA and the nucleic acid binding domains are DNA-binding domains] one nucleic acid-binding domain includes a zinc finger motif and the other nucleic acid-binding domain includes a motif or domain selected from the group consisting of a helix-loop-helix motif, a helix-turn-helix motif, and a basic domain.
42. (Amended) The nucleic acid of claim 41, wherein [one DNA-binding domain is selected from the group consisting of a homeodomain. a] the zinc finger [domain, a basic region/helix-loop-helix (bHLH) domain, a helix-turn-helix domain, a leucine zipper, a DNA binding domain of a steroid receptor and variants thereof] motif is from a protein selected from the group consisting of transcription factor IIIA, SW15, Kruppel, Hunchback, and a steroid receptor.
43. (Amended) The nucleic acid of claim [42] 41, wherein [one DNA-binding domain is a homeodomain] the zinc finger motif is from Zif268.
44. (Amended) The nucleic acid of claim [42] 40, wherein [one DNA-binding domain is a zinc finger] one nucleic acid-binding domain includes a zinc finger motif and the other nucleic acid-binding domain includes a helix-turn-helix motif.
45. (Amended) The nucleic acid of claim 44, [further comprising] wherein the other nucleic acid-binding domain includes a homeodomain.
46. (Amended) The nucleic acid of claim [43] 45, wherein the homeodomain is [from] an Oct-1 [protein] homeodomain [or variants thereof].
47. (Amended) The nucleic acid of claim 46, wherein the zinc finger motif is from a protein selected from the group consisting of transcription factor IIIA, Zif268, SW15, Kruppel, Hunchback, and [variants thereof] a steroid receptor.

- 48 (Amended) The nucleic acid of claim [45] 47, wherein the homeodomain is [from] an Oct-1 [protein] homeodomain and the zinc finger [domain] motif is from Zif268
- 49 (Amended) The nucleic acid of claim 48, wherein the chimeric protein further comprises a second zinc finger[s 1 and 2] of Zif268 [a glycine-glycine-arginine-arginine linker and an Oct-1 homeodomain]
- 50 (Amended) The nucleic acid of claim [48] 49, which encodes ZFHDI
- 51 (Amended) The nucleic acid of claim [42] 41, wherein the [bHLH] the other nucleic acid-binding domain is from a protein selected from the group consisting of Da daughterless, Achaete-scute (T3), MyoD, and E12 E47 [and variants thereof].
- 52 (Amended) The nucleic acid of claim [42] 41, wherein [the helix-turn-helix] the other nucleic acid-binding domain is from a protein selected from the group consisting of MAT  $\alpha$ 1, MAT  $\alpha$ 2, MAT  $\alpha$ 1, Antennapedia, Ultrabithorax, Engrailed, Paired, Fushi tarazu, HOX, Unc86, Oct1, Oct2, and Pit [and variants thereof].
- 53 (Amended) The nucleic acid of claim [42] 41, wherein the [leucine zipper one DNA binding] other nucleic acid-binding domain is from a protein selected from the group consisting of GCN4, C/EBP, c-Fos, c-Jun, and JunB [and variants thereof]
- 54 (Amended) The nucleic acid of claim [42] 41, wherein the zinc finger motif is from a [the] steroid receptor [is a glucocorticoid receptor or variants thereof]
- 55 (Amended) The nucleic acid of claim 40, wherein the [first and second] two nucleic acid-binding domains are separated by at least one amino acid
- 56 (Amended) The nucleic acid of claim 40, wherein the chimeric protein binds with higher affinity to the composite binding site than to each of the portions of the composite binding site to which each of the [first and the second] two nucleic acid binding domains bind.
- 57 (Amended) The nucleic acid of claim 40, wherein the chimeric protein further comprises [an additional] a functional domain.

- Subj 58*
- (Amended) The nucleic acid of claim 57, wherein the [additional] functional domain is a regulatory domain
59. The nucleic acid of claim 58, wherein the regulatory domain is an activation domain
60. The nucleic acid of claim 59, wherein the activation domain is an Herpes Simplex Virus VP16 activation domain
61. The nucleic acid of claim 58, wherein the ~~regulatory~~ domain is a repression domain.
62. The nucleic acid of claim 61, wherein the repression domain is from a Kruppel protein.
- Subj 63*
- (Amended) The nucleic acid of claim 57, wherein the [additional] functional domain is a nucleic acid cleavage domain.
64. The nucleic acid of claim 63, wherein the ~~nucleic acid cleavage~~ domain is the FokI cleavage domain.
- Subj 65*
- (Amended) The nucleic acid of claim 57, wherein the [additional] functional domain is selected from the group consisting of a domain interacting with a cellular component, a domain which controls the stability of the chimeric protein, and a domain which controls subcellular localization.
66. (Amended) A nucleic acid encoding a chimeric protein which binds a nucleic acid comprising a composite binding site, wherein the chimeric protein comprises [at least] two nucleic acid-binding domains, [referred to as the first domain and the second domain.] each of which binds a sequence which is a portion of the composite binding site, wherein only one of the two nucleic acid-binding domains includes a DNA binding domain from a protein comprising a homeodomain, and which [first and second] nucleic acid-binding domains
- (i) do not occur in the same protein in nature;
  - (ii) do not occur in the same protein in nature in the order in which they are present in the chimeric protein; and/or
  - (iii) do not occur in nature with the same spacing that is present in the chimeric protein[.
- and wherein the chimeric protein further comprises an additional domain]

67. (Amended) The nucleic acid of claim 66, wherein [the additional domain is a regulatory domain] one nucleic acid-binding domain includes a helix-turn-helix motif and the other nucleic acid-binding domain includes a motif or domain selected from the group consisting of a zinc finger motif, a helix-loop-helix motif, and a basic domain
68. (Amended) The nucleic acid of claim [67] 66, wherein the chimeric protein further comprises [regulatory domain is] an activation domain
69. (Amended) The nucleic acid of claim [68] 66, wherein the [regulatory domain is] chimeric protein further comprises a repression domain.
70. (Amended) The nucleic acid of claim 66, wherein the [additional domain is] chimeric protein further comprises a nucleic acid cleavage domain.
71. (Canceled) A nucleic acid encoding a transcription factor comprising an activation domain and a chimeric nucleic acid binding domain which binds a nucleic acid comprising a composite binding site, wherein the chimeric nucleic acid binding domain comprises a first domain and a second domain, each of which binds a sequence which is a portion of the composite binding site, and which first and second domains
- (i) do not occur in the same protein in nature;
  - (ii) do not occur in the same protein in nature in the order in which they are present in the chimeric protein; and/or
  - (iii) do not occur in nature with the same spacing that is present in the chimeric protein.
72. (Amended) A vector comprising a nucleic acid of [any one of] claim[s] 40.
73. (Amended) The vector of claim 72, further comprising expression control sequences permitting gene expression in eukaryotic cells.
74. A kit comprising a nucleic acid of claim 72 and a gene operably linked to a composite binding site to which the chimeric protein encoded by the vector binds.
75. A method for modulating expression of a gene in a cell, comprising [modulating the level of] expressing a chimeric protein in a cell which includes a gene operably linked to a composite binding site to which the chimeric protein binds, wherein the chimeric protein comprises [at

- least] two nucleic acid-binding domains, [referred to as the first domain and the second domain,] each of which binds a sequence which is a portion of the composite binding site, and
- which [first and second] nucleic acid-binding domains
    - (i) do not occur in the same protein in nature,
    - (ii) do not occur in the same protein in nature in the order in which they are present in the chimeric protein; and or
    - (iii) do not occur in nature with the same spacing that is present in the chimeric protein,

whereby the chimeric protein binds the composite binding site, thereby modulating expression of the gene in the cell.

76. (Amended) The method of claim 75, wherein the chimeric protein further comprises a[n additional] functional domain.

77. (Amended) The method of claim 76, wherein the [additional] functional domain is a regulatory domain.

78. The method of claim 77, wherein the regulatory domain is an activation domain.

79. The method of claim 78, wherein the activation domain is an Herpes Simplex Virus VP16 activation domain.

80. The method of claim 77, wherein the regulatory domain is a repression domain.

81. (Amended) The method of claim 75, wherein [one nucleic acid-binding] one nucleic acid-binding domain includes a zinc finger motif and the other nucleic acid-binding domain [is] includes a motif or domain selected from the group consisting of [a homeodomain, a zinc finger domain,] a basic domain [region/], a helix-loop-helix [(bHLH) domain] motif, and a helix-turn-helix motif [domain, a leucine zipper, a DNA binding domain of a steroid receptor and variants thereof].

82. (Amended) The method of claim 81, wherein [one nucleic acid-binding] the other domain is a homeodomain.

- 83 (Amended) The method of claim [81] 75, wherein [one nucleic acid binding domain is a zinc finger domain] the chimeric protein further comprises an additional nucleic acid-binding domain, which binds a sequence which is a portion of the composite binding site
- 84 (Amended) The method of claim 83, wherein the additional [chimeric protein further comprises a homeodomain] nucleic acid-binding domain includes a zinc finger motif
- 85 A method for producing a cell for use in the method of claim 75, comprising introducing into a cell a nucleic acid encoding the chimeric protein
- 86 A method for producing a cell for use in the method of claim 75, comprising introducing into a cell a nucleic acid comprising a composite binding site
- 87 The method of claim 86, further comprising introducing into the cell a nucleic acid encoding the chimeric protein.
- 88 The method of claim 87, wherein the gene encodes a recombinant gene product.

Please add new claims 89-97:

- 89 The nucleic acid of claim 66, wherein one nucleic acid-binding domain includes a homeodomain.
- 90 The nucleic acid of claim 40, further comprising an additional nucleic acid-binding domain, which binds a sequence which is a portion of the composite binding site.
- 91 The nucleic acid of claim 66, further comprising an additional nucleic acid-binding domain, which binds a sequence which is a portion of the composite binding site.
- 92 The nucleic acid of claim 71 further comprising an additional nucleic acid-binding domain, which binds a sequence which is a portion of the composite binding site.
- 93 The nucleic acid of claim 75, further comprising an additional nucleic acid-binding domain, which binds a sequence which is a portion of the composite binding site.